DETAILED ACTION

Election/Restrictions

1. This action is in response to a response to a restriction requirement filed on November 30, 2007. Applicant's election without traverse of Group V in the reply filed on November 30, 2007 is acknowledged. There are twenty-two claims pending and twelve under consideration. Claims 7-9 and 14-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 30, 2007. This is the first action on the merits. The application concerns a novel group of 4-phenylpiperidine derivatives, their compositions, and their use as a renin inhibitor. Since the election was made without traverse, the restriction requirement is deemed proper and therefore made **FINAL**.

Priority

2. This application is a non-provisional application 10/580,296, filed on May 23, 2006 and is a national stage entry of PCT/EP04/13410, filed on November 25, 2004, which claims domestic priority to U.S. Provisional Application No. 60/525375, filed on November 28, 2003.

Specification

3. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any of the errors of which applicant may become aware of in the specification.

Claim Objections

5. Claims 6 and 12 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Once Claims 5 and 11 are rewritten in light of the elected subject matter from the restriction requirement, Claims 6 and 12 will be substantial duplicates of Claims 5 and 11 and will not further limit the Claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21 and 12 claim, “A pharmaceutical composition comprising a pharmaceutically effective amount of a compound of Claim 1…” without defining what the composition is treating. The language of Claims 21 and 22 are written in such a way as to claim an “effective amount” without explicitly defining what disease or disorder it is treating, which is not permitted. The claims are indefinite and need to be rewritten.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

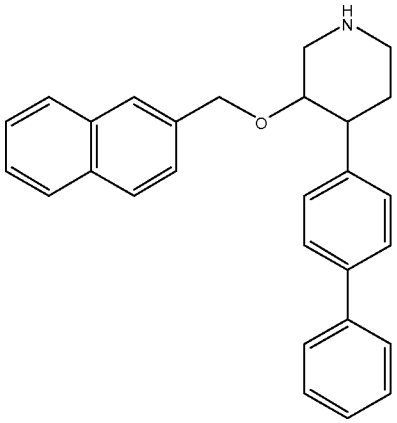
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

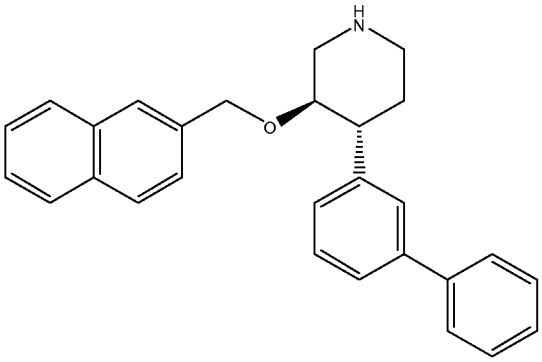
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1- 6, 10-13, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhisetti et. al. (WO2002088101) in view of In re *Norris* (CCPA 1950) 179 F2d 970, 84 USPQ 458. The current application recites a variety of compounds for use as a renin inhibition whereas the prior art recites a variety of compounds used for BACE inhibition.

Bhisetti et. al. defines Registry No. 474332-67-7 (See STN search report) or 4-(biphenyl-4-yl)-3-(naphthalen-2-ylmethoxy)piperidine seen on the next page:



Whereas the current application elects as its species the compound of (3R,4R)-4-(biphenyl-3-yl)-3-(naphthalen-2-ylmethoxy)piperidine seen here:



Chemically, the two structures differ in that the biphenyl group is a para-substituted biphenyl group in the prior art, but is meta-substituted biphenyl group in the current application.

Bhisetti, et. al. cites BACE inhibitors as a use for their compounds and compositions while the current application has a suggested use for its compounds and compositions as renin inhibitors. It is well known in the chemical arts that both BACE and renin proteases fall under the same broader category of aspartic proteases. Thus,

both the prior art and the current application have a suggested use for their compounds and compositions as aspartic protease inhibitors.

Bhisetti, et. al. recites the synthesis of "4-biphenyl-4-yl-3-(napthalen-2-ylmethoxy)-piperidine" which chemically is the same as "4-(biphenyl-4-yl)-3-(naphthalen-2-ylmethoxy)piperidine" seen above. (See Specification, page 175, Example 401). While the current application claims a particular stereoisomer, Bhisetti, et. al. does not, and is therefore presumed to be the racemic mixture of the isomers as no mention is made of structure geometry.

Compounds having the same radical at different positions on the nucleus are position isomers. Their properties are often so nearly alike as to present difficulties in identification or separation. Ex *parte Mowry*(POBA 1950) 91 USPQ 219. A novel, useful compound which is isomeric with a compound of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compound. In re *Norris* (CCPA 1950) 179 F2d 970, 84 USPQ 458; *In re Finley* (CCPA 1949) 174 F2d 130 and 135, 81 USPQ 383 and 387. Similarly, an optically active isomer is unpatentable over a prior art racemate or optical Isomer of opposite rotation in the absence of unexpected or unobvious beneficial properties. *In re Adamson* et aL (CCPA 1960) 275 F2d 952, 125 USPQ 233; *Brenner et al. v. Ladd, Comr. Pats.* (DCDC 1965) 247 FSupp 51, 147 USPQ 87.

It would have been obvious to one skilled in the arts at the time of the invention to be motivated to combine Bhisetti, et. al. and the case law of *In re Norris* to synthesize the compound, 4-(biphenyl-3-yl)-3-(naphthalen-2-ylmethoxy)piperidine or a composition

comprising the compound 4-(biphenyl-3-yl)-3-(naphthalen-2-ylmethoxy)piperidine for use as an aspartic protease inhibitor such as a BACE or renin inhibitor.

Bhisetti et. al. combined with *In re Norris* shows the necessary teachings that suggest shifting the biphenyl from the para-position to the meta-position in an attempt to enhance activity and afford a positive benefit from the replacement.

Double Patenting

11. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

12. Claims 6 and 12 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 5 and 11. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Once Claims 5 and 11 are rewritten in light of the elected subject matter from the restriction requirement, Claims 6 and 12 will be substantial duplicates of Claims 5 and 11. Appropriate correction is required.

Conclusion

13. Claims 1-6, 10-13, 21, and 22 are rejected.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on Mon.-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H. Murray/

/James O. Wilson/
Supervisory Patent Examiner
Art Unit 1624